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Seminar Schedule - N. America

NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	JUL 12	BEILSTEIN enhanced with new display and select options, resulting in a closer connection to BABS
NEWS 4	AUG 02	IFIPAT/IFIUDB/IFICDB reloaded with new search and display fields
NEWS 5	AUG 02	CAplus and CA patent records enhanced with European and Japan Patent Office Classifications
NEWS 6	AUG 02	The Analysis Edition of STN Express with Discover! (Version 7.01 for Windows) now available
NEWS 7	AUG 27	BIOCOMMERCE: Changes and enhancements to content coverage
NEWS 8	AUG 27	BIOTECHABS/BIOTECHDS: Two new display fields added for legal status data from INPADOC
NEWS 9	SEP 01	INPADOC: New family current-awareness alert (SDI) available
NEWS 10	SEP 01	New pricing for the Save Answers for SciFinder Wizard within STN Express with Discover!
NEWS 11	SEP 01	New display format, HITSTR, available in WPIDS/WPINDEX/WPIX
NEWS 12	SEP 27	STANDARDS will no longer be available on STN
NEWS 13	SEP 27	SWETSCAN will no longer be available on STN
NEWS 14	OCT 28	KOREAPAT now available on STN

NEWS EXPRESS	OCTOBER 29 CURRENT WINDOWS VERSION IS V7.01A, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

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FILE 'HOME' ENTERED AT 16:56:52 ON 08 NOV 2004

=> index bioscience
FILE 'DRUGMONOG' ACCESS NOT AUTHORIZED

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FULL ESTIMATED COST	0.21	0.21

INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, ANTE, AQUALINE, AQUASCI, BIOBUSINESS, BIOCOMMERCE, BIOENG, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE, DISSABS, ...' ENTERED AT 16:57:08 ON 08 NOV 2004

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=> bcl-2 and nmr and apoptosis
          1   FILE ADISINSIGHT
          2   FILE AGRICOLA
          1   FILE BIOENG
         22   FILE BIOSIS
  12 FILES SEARCHED...
          2   FILE BIOTECHABS
          2   FILE BIOTECHDS
          8   FILE BIOTECHNO
         10   FILE CANCERLIT
         29   FILE CAPLUS
          1   FILE CEABA-VTB
          1   FILE CIN
          3   FILE DDFU
          3   FILE DISSABS
          5   FILE DRUGU
  31 FILES SEARCHED...
         21   FILE EMBASE
         15   FILE ESBIOBASE
          3   FILE FEDRIP
          1   FILE FSTA
          6   FILE IFIPAT
          4   FILE JICST-EPLUS
          6   FILE LIFESCI
         25   FILE MEDLINE
  50 FILES SEARCHED...
          3   FILE NTIS
          7   FILE PASCAL
          1   FILE PROMT
  61 FILES SEARCHED...
         44   FILE SCISEARCH
          8   FILE TOXCENTER
        466   FILE USPATFULL
         44   FILE USPAT2
          2   FILE WPIDS
  73 FILES SEARCHED...
          2   FILE WPINDEX

  31 FILES HAVE ONE OR MORE ANSWERS,   75 FILES SEARCHED IN STNINDEX

L1   QUE BCL-2 AND NMR AND APOPTOSIS

=> file caplus biosis medline
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                               3.42       3.63

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=> dup remove
ENTER L# LIST OR (END):end
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=> bcl-2 and nmr and apoptosis
L2          76 BCL-2 AND NMR AND APOPTOSIS

=> dup remove
ENTER L# LIST OR (END):l2
PROCESSING COMPLETED FOR L2
L3           43 DUP REMOVE L2 (33 DUPLICATES REMOVED)

=> d ti 23-43

L3   ANSWER 23 OF 43  BIOSIS  COPYRIGHT (c) 2004 The Thomson Corporation.  on
     STN
TI   Novel chemically-stabilized helices of the BCL-2
     family induce apoptosis of leukemia cells.

L3   ANSWER 24 OF 43  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Phospholipid scramblase transport system-based method for targeting
     chemical compounds to cells, pharmaceutical compositions, and therapeutic
     and diagnostic use

L3   ANSWER 25 OF 43  CAPLUS  COPYRIGHT 2004 ACS on STN
TI   Preparation of amino acid derivatives used as perturbed membrane-binding
     compounds for diagnostic and therapeutic applications

L3   ANSWER 26 OF 43     MEDLINE on STN
TI   The apoptotic protein tBid promotes leakage by altering membrane
     curvature.

L3   ANSWER 27 OF 43  CAPLUS  COPYRIGHT 2004 ACS on STN DUPLICATE 11
TI   Novel Polyphenol Molecule Isolated from Licorice Root (Glycyrrhiza glabra)
     Induces Apoptosis, G2/M Cell Cycle Arrest, and Bcl-
     2 Phosphorylation in Tumor Cell Lines

L3   ANSWER 28 OF 43  BIOSIS  COPYRIGHT (c) 2004 The Thomson Corporation.  on
     STN
TI   A view to a kill: Ligands for Bcl-2 family proteins.

L3   ANSWER 29 OF 43  CAPLUS  COPYRIGHT 2004 ACS on STN DUPLICATE 12
TI   Changes in phosphate metabolism in thymoma cells suggest mechanisms for
     resistance to dexamethasone-induced apoptosis. A 31P NMR
     spectroscopic study of cell extracts

L3   ANSWER 30 OF 43     MEDLINE on STN
TI   Backbone dynamics of the 8 kDa dynein light chain dimer reveals molecular
     basis of the protein's functional diversity.

L3   ANSWER 31 OF 43  CAPLUS  COPYRIGHT 2004 ACS on STN DUPLICATE 13
TI   Novel substituted methylenedioxy lignan suppresses proliferation of cancer
     cells by inhibiting telomerase and activation of c-myc and caspases
     leading to apoptosis

L3   ANSWER 32 OF 43  CAPLUS  COPYRIGHT 2004 ACS on STN DUPLICATE 14
TI   What's in the 'BAG'? - a functional domain analysis of the BAG-family
     proteins

L3   ANSWER 33 OF 43  CAPLUS  COPYRIGHT 2004 ACS on STN DUPLICATE 15
TI   Discovery of Small-Molecule Inhibitors of Bcl-2
     through Structure-Based Computer Screening
```

L3 ANSWER 34 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI Bax and other pro-apoptotic **Bcl-2** family "killer-proteins" and their victim, the mitochondrion.

L3 ANSWER 35 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 16
TI Identification of small-molecule inhibitors of interaction between the BH3 domain and Bcl-XL

L3 ANSWER 36 OF 43 MEDLINE on STN
TI **NMR** studies of the anti-apoptotic protein Bcl-xL in micelles.

L3 ANSWER 37 OF 43 MEDLINE on STN
TI Rationale for Bcl-xL/Bad peptide complex formation from structure, mutagenesis, and biophysical studies.

L3 ANSWER 38 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI Targeting the mitochondrial redox state of leukemia and lymphoma cells with PK11195 for effective therapy.

L3 ANSWER 39 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI Assessing pore formation by **BCL-2** during **apoptosis** in cell lines and human leukemic cells: Cysteine 158 in the alpha 5 helical loop is in an aqueous environment.

L3 ANSWER 40 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 17
TI Refolding, Purification, and Characterization of a Loop Deletion Mutant of Human **Bcl-2** from Bacterial Inclusion Bodies

L3 ANSWER 41 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 18
TI Recombinant mouse **Bcl-2**(1-203). Two domains connected by a long protease-sensitive linker

L3 ANSWER 42 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 19
TI Detection of apoptotic cell death by proton nuclear magnetic resonance spectroscopy

L3 ANSWER 43 OF 43 MEDLINE on STN
TI X-ray and **NMR** structure of human Bcl-xL, an inhibitor of programmed cell death.

=> ti 1-23
L4 1 TI 1-23

=> d ti 1-23

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN
TI Separating commercially pure vanadium from crude ferrophosphorus

=> bcl-2 and nmr and apoptosis
L5 76 BCL-2 AND NMR AND APOPTOSIS

=> dup re,ove
'RE' IS NOT VALID HERE

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Enter "REMOVE" to identify and remove duplicate answers.
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=> dup remove l5
PROCESSING COMPLETED FOR L5
L6 43 DUP REMOVE L5 (33 DUPLICATES REMOVED)

=> d ti 1-23

L6 ANSWER 1 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
TI Conversion of apoptotic proteins

L6 ANSWER 2 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
TI Methods of identifying agents that alter association of Bit1 and AES, alter **Bcl-2** transcription, and/or modulate cell death, and therapeutic uses

L6 ANSWER 3 OF 43 MEDLINE on STN
TI Conformation of membrane-associated proapoptotic tBid.

L6 ANSWER 4 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
TI Changes in phosphate metabolism in thymoma cells suggest mechanisms for resistance to dexamethasone-induced **apoptosis**. A 31P **NMR** spectroscopic study of cell extracts. [Erratum to document cited in CA138:036909]

L6 ANSWER 5 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
TI Solution Conformations of Wild-Type and Mutated Bak BH3 Peptides via Dynamical Conformational Sampling and Implication to Their Binding to Antiapoptotic **Bcl-2** Proteins

L6 ANSWER 6 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1
TI Targeting **Apoptosis** via Chemical Design Inhibition of Bid-Induced Cell Death by Small Organic Molecules

L6 ANSWER 7 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 2
TI Divergence of Genbank and human tumor **Bcl-2** sequences and implications for binding affinity to key apoptotic proteins

L6 ANSWER 8 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 3
TI Localization of dynein light chains 1 and 2 and their pro-apoptotic ligands

L6 ANSWER 9 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 4
TI Rational design and real time, in-cell detection of the proapoptotic activity of a novel compound targeting Bcl-XL

L6 ANSWER 10 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 5
TI Small-molecule inhibitors of **Bcl-2** protein

L6 ANSWER 11 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 6
TI Structural studies of **apoptosis** and ion transport regulatory proteins in membranes

L6 ANSWER 12 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 7
TI Defining the p53 DNA-binding domain/Bcl-xL-binding interface using

NMR

L6 ANSWER 13 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 8
TI Overexpression of catalase or **Bcl-2** alters glucose and energy metabolism concomitant with dexamethasone resistance

L6 ANSWER 14 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
TI Humanin protein interactions with Bax and Bid and their use for identifying modulators of **apoptosis**

L6 ANSWER 15 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
TI Solution Structure of Human BCL-w: Modulation of Ligand Binding by the C-Terminal Helix

L6 ANSWER 16 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
TI Discovery, Characterization, and Structure-Activity Relationships Studies of Proapoptotic Polyphenols Targeting B-Cell Lymphocyte/Leukemia-2 Proteins

L6 ANSWER 17 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
TI Cyclic AMP reverses radiocontrast media-induced **apoptosis** in LLC-PK1 cells by activating A kinase/PI3 kinase

L6 ANSWER 18 OF 43 MEDLINE on STN
TI Unique structural features of a **BCL-2** family protein CED-9 and biophysical characterization of CED-9/EGL-1 interactions.

L6 ANSWER 19 OF 43 MEDLINE on STN
TI Solution structure of the BHRF1 protein from Epstein-Barr virus, a homolog of human **Bcl-2**.

L6 ANSWER 20 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI Interaction of BID, a pro-apoptotic **BCL-2** family member, with lipid membranes: A site-directed spin labeling Study.

L6 ANSWER 21 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 9
TI Overexpression of catalase or **Bcl-2** delays or prevents alterations in phospholipid metabolism during glucocorticoid-induced **apoptosis** in WEHI7.2 cells

L6 ANSWER 22 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 10
TI Structure determination, **apoptosis** induction, and telomerase inhibition of CFP-2, a novel lichenin from Cladonia furcata

L6 ANSWER 23 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI Novel chemically-stabilized helices of the **BCL-2** family induce **apoptosis** of leukemia cells.

=> d ab bib 20, 22, 23, 28, 39, 40

L6 ANSWER 20 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 2003:422995 BIOSIS
DN PREV200300422995
TI Interaction of BID, a pro-apoptotic **BCL-2** family member, with lipid membranes: A site-directed spin labeling Study.

AU Oh, Kyoung Joon [Reprint Author]; Meyer, Natalie [Reprint Author]; Korsmeyer, Stanley J. [Reprint Author]
CS Harvard Medical School, Dana-Farber Cancer Institute, HHMI, 44 Binney St., Smith 758, Boston, MA, 02115-7008, USA
SO Biophysical Journal, (February 2003) Vol. 84, No. 2 Part 2, pp. 205a-206a. print.
Meeting Info.: 47th Annual Meeting of the Biophysical Society. San Antonio, TX, USA. March 01-05, 2003. Biophysical Society.
ISSN: 0006-3495 (ISSN print).
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 17 Sep 2003
Last Updated on STN: 17 Sep 2003

L6 ANSWER 22 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 10
AB A great deal of exptl. evidence has accumulated in the past several decades, suggesting that polysaccharides have wide bioactivities. Cladonia furcata polysaccharide, CFP-2, a water-soluble lichenin with a mean Mr 7.6 + 104, was first obtained by 0.25 M NaOH solution extraction, ethanol precipitation, DEAE-cellulose, and Sephadex G-200 column chromatog. Gas chromatog. of acid hydrolyzate of CFP-2 suggested that it was composed of D-glucose, D-galactose, and D-mannose in the molar ratios of 8:1:1. Periodate oxidation, Smith degradation, IR, and **NMR** spectroscopy anal. revealed that CFP-2 had a backbone consisting of α-(1→3) and α-(1→4)-linked D-glucopyranosyl residues substituted at O-6 with β-(1→6)-linked D-galactopyranosyl residue and α-(1→6)-linked D-mannopyranosyl residue. CFP-2 was able to reduce viability of cultured HL-60 and K562 cells. The antiproliferative properties of CFP-2 appeared to be attributable to its induction of apoptotic cell death as determined by ultrastructural change, internucleosomal DNA fragmentation, and increased proportion of the subdiploid cell population. To elucidate mol. events in the **apoptosis**, protein expressions of **Bcl-2**, Bax, Fas, and FasL were measured by Western blotting using specific antibodies in HL-60 cells. The level of **Bcl-2** remained largely unchanged, but the Bax, Fas, and FasL expression showed up-regulation. Moreover, the telomerase activity analyzed by TRAP-ELISA assay in HL-60 cells treated with CFP-2 decreased as compared with the untreated control cells. These results suggest that CFP-2 could have a possible cancer therapeutic potential.
AN 2003:567406 CAPLUS
DN 139:334572
TI Structure determination, **apoptosis** induction, and telomerase inhibition of CFP-2, a novel lichenin from Cladonia furcata
AU Lin, Xin; Cai, Yu-Jun; Li, Zhi-Xiao; Chen, Qian; Liu, Zhong-Li; Wang, Rui
CS School of Life Science, Department of Biochemistry and Molecular Biology, Lanzhou University, Lanzhou, 730000, Peop. Rep. China
SO Biochimica et Biophysica Acta (2003), 1622(2), 99-108
CODEN: BBACAQ; ISSN: 0006-3002
PB Elsevier Science B.V.
DT Journal
LA English
RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 23 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AB Faulty regulation of apoptotic pathways is a seminal event in the pathogenesis of a wide variety of hematologic, oncologic, and other

diseases. **Apoptosis** is governed by the **BCL-2** family of pro- and anti-apoptotic proteins, which form a complex network of checks and balances that dictate cell fate. **BCL-2**, for example, is a survival protein whose overproduction can facilitate pathologic cell survival. Anti-apoptotic proteins, such as **BCL-2** and BCL-XL, and pro-apoptotic proteins, such as BAK and BAX, share sequence conservation in multiple "**BCL-2** homology" (BH) domains. These "multidomain" apoptotics exert their roles as guardian or executioner at mitochondrial and endoplasmic reticulum membranes, receiving regulatory signals from another class of pro-apoptotic proteins, characterized by homology in the BH3-domain only. Deletion and mutagenesis studies determined that the amphipathic alpha-helical BH3 segment of pro-apoptotic family members functions as a critical death domain. Whereas peptides modeled after BH3 domains retain select in vitro biochemical activities, their in vivo utility is compromised by loss of helical secondary structure, susceptibility to proteolytic degradation, and inability to penetrate intact cells. We developed and applied a chemical strategy for generating highly specific and stable peptidic compounds that preserve both the primary and secondary structure of biologically active apoptotic peptides, in order to maximize their potential as therapeutic reagents and as in vivo biological tools to elucidate apoptotic pathways. We employed a synthetic crosslinking strategy to generate a panel of "Stabilized Alpha-Helices of BH3-domains" or SAHBs modeled after the BH3 domain of BID, a pro-apoptotic family member capable of activating mitochondrial cell death through interactions with both pro- and anti-apoptotic multidomain proteins. Circular dichroism studies revealed dramatic enhancement of SAHB secondary structure in solution, with several compounds displaying a more than 5-fold increase in percent helicity compared to the unmodified BID BH3 peptide. SAHBs are likewise more resistant to proteolytic degradation as determined by trypsin digestion kinetic analyses. In in vitro binding assays, SAHBs display increased **BCL-2** binding affinity. Two-dimensional 1H-15N Heteronuclear Single Quantum Correlation Nuclear Magnetic Resonance (HSQC **NMR**) spectra confirmed that SAHBs specifically engage the physiologic BH3-binding site of multidomain anti-apoptotic proteins. SAHBs induce rapid release of cytochrome c from purified mouse liver mitochondria, but have no effect on mitochondria lacking BAK/BAX, confirming the specificity of SAHB activity in triggering mitochondrial **apoptosis**. The cell permeability of SAHBs was demonstrated by tracking fluorescein-labeled SAHBs in cultured cells by FACS analysis and confocal microscopy. Furthermore, SAHBs activate **apoptosis** in cultured B-, T-, and mixed-lineage leukemia cells. The specificity of SAHB activity in inducing leukemia cell **apoptosis** was confirmed by the inability of mutant SAHBs, incorporating a single point mutation known to abolish BH3-domain activity, to have any effect on the cultured cells. These data indicate that SAHBs have the potential to serve as biological tools to dissect and manipulate apoptotic pathways in vivo in normal and malignant cells.

AN 2004:180831 BIOSIS

DN PREV200400180880

TI Novel chemically-stabilized helices of the **BCL-2** family induce **apoptosis** of leukemia cells.

AU Walensky, Loren D. [Reprint Author]; Escher, Iris; Malia, Thomas J.; Wagner, Gerhard; Verdine, Gregory L.; Korsmeyer, Stanley J.

CS Department of Pediatric Hematology/Oncology, Dana Farber Cancer Institute/Children's Hospital Boston, Harvard Medical School, Boston, MA, USA

SO Blood, (November 16 2003) Vol. 102, No. 11, pp. 5a. print. Meeting Info.: 45th Annual Meeting of the American Society of Hematology.

San Diego, CA, USA. December 06-09, 2003. American Society of Hematology. CODEN: BLOOAW. ISSN: 0006-4971.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 7 Apr 2004
Last Updated on STN: 7 Apr 2004

L6 ANSWER 28 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 2002:500148 BIOSIS
DN PREV200200500148
TI A view to a kill: Ligands for **Bcl-2** family proteins.
AU Rutledge, Stacey E. [Reprint author]; Chin, Jasòn W.; Schepartz, Alanna [Reprint author]
CS Department of Chemistry, Yale University, PO Box 208107, New Haven, CT, 06520-8107, USA
SO Current Opinion in Chemical Biology, (August, 2002) Vol. 6, No. 4, pp. 479-485. print.
ISSN: 1367-5931.
DT Article
General Review; (Literature Review)
LA English
ED Entered STN: 25 Sep 2002
Last Updated on STN: 25 Sep 2002

L6 ANSWER 39 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AB The ability of the **Bcl-2** family of anti-apoptotic proteins to prevent programmed cell death has been attributed to multiple mechanisms, including binding pro-apoptotic proteins as well as the formation of pores. The evidence for the latter mechanism is extensive but indirect and includes the presence of alpha helical domains (designated alpha-5 and alpha-6) that are similar to several bacterial pore forming domains, as determined by **NMR** and X-ray crystallography of recombinant Bcl-XL without the hydrophobic insertion tail; the ability of recombinant Bcl-XL and **Bcl-2** to form ion conducting channels in artificial lipid bi-layers; and the loss of anti-apoptotic activity of a Bcl-XL mutant in which a portion of the putative pore forming domain is altered. To assess the conformation of **Bcl-2**, we have examined the local environment of cysteine 158 located in the alpha-5 helix near the base of the pore forming region, and cysteine 229 located in the hydrophobic insertion sequence, using the lipid impermeant cysteine modifying agent iodoacetylamino stilbene disulfonic acid (IASD). When human **Bcl -2** is translated in vitro in the absence of membranes, both cysteines are modified by IASD, albeit with different kinetics. In the presence of membranes, cysteine 229 is not labelled by IASD, consistent with our previous work demonstrating that the insertion sequence is necessary and sufficient for insertion into multiple intracellular membranes. In this circumstance, cysteine 158 is still modifiable by IASD. In the Rat 1/myc model system of **apoptosis**, cysteine 158 is accessible to IASD in untreated cells, and early during serum starvation-induced **apoptosis** at time points during which **Bcl-2** is protective. By contrast, late in **apoptosis** when **Bcl-2** has lost its effect, this cysteine is no longer modifiable. Cysteine 229 remains inaccessible under all three conditions, consistent with the expected membrane topology of **Bcl-2** in cells. Ongoing experiments will assess whether

a functionally active Bcl-XL mutant targeted to the endoplasmic reticulum in human breast cancer MCF7 cells, and endogenous **Bcl-2** in the lymphocytes of patients with B cell chronic lymphocytic leukemia adopt a similar configuration. Our results suggests that the alpha-5 helical loop is not in a lipid environment while **Bcl-2** is functioning to prevent **apoptosis**.

AN 2001:289142 BIOSIS
DN PREV200100289142
TI Assessing pore formation by **BCL-2** during **apoptosis** in cell lines and human leukemic cells: Cysteine 158 in the alpha 5 helical loop is in an aqueous environment.
AU Leber, B. [Reprint author]; Kim, P. [Reprint author]; Falcone, D. [Reprint author]; Annis, M. [Reprint author]; Andrews, D. W. [Reprint author]
CS Medicine, McMaster University, Hamilton, ON, Canada
SO Blood, (November 16, 2000) Vol. 96, No. 11 Part 2, pp. 174b. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology. San Francisco, California, USA. December 01-05, 2000. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 20 Jun 2001
Last Updated on STN: 19 Feb 2002

L6 ANSWER 40 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 17
AB This report describes the cloning of recombinant human **Bcl-2**, in which the putative disordered loop region has been replaced with a flexible linker and the hydrophobic C-terminus has been replaced with a 6xHis tag (**Bcl-2**(6-32)-AAAA-**Bcl-2**(86-206)-HHHHHH, abbreviation rhBcl-2; amino acid numbering excludes the initiating methionine). This protein was expressed in Escherichia coli, where it accumulated in insol. form in inclusion bodies. After lysis, the washed inclusion bodies were solubilized and an L-arginine assisted protein refolding route was employed to obtain biol. active protein. RhBcl-2 was purified further by nickel chelate chromatog. to give protein of >95% purity, with an overall yield of 5 mg per g of E. coli cell paste. Edman sequencing showed that .apprx.90% of the rhBcl-2 retained the initiating methionine residue. Anal. size exclusion chromatog. suggested that the refolded and purified rhBcl-2 was monomeric in nondenaturing solution Purified protein had an affinity for a Bax BH3 domain peptide comparable to that for in vivo folded recombinant human **Bcl-2** and suppressed caspase activation in a cell-free assay for **apoptosis**. 1H **NMR** spectroscopy of rhBcl-2, both free and complexed with the Bax BH3 domain peptide, provided further evidence for the structural and functional integrity of the refolded protein. These findings parallel and extend those of Muchmore et al., who found that a loop deletion mutant of human Bcl-XL retained anti-apoptotic function. (c) 1999 Academic Press.
AN 1999:134162 CAPLUS
DN 131:4284
TI Refolding, Purification, and Characterization of a Loop Deletion Mutant of Human **Bcl-2** from Bacterial Inclusion Bodies
AU Anderson, Malcolm; Blowers, David; Hewitt, Neil; Hedge, Philip; Breeze, Alexander; Hampton, Ian; Taylor, Ian
CS Target Discovery, Zeneca Pharmaceuticals, Macclesfield, SK10 4TG, UK
SO Protein Expression and Purification (1999), 15(2), 162-170
CODEN: PEXPEJ; ISSN: 1046-5928
PB Academic Press

DT Journal
LA English
RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE

08/11/200414:05Print selected from Online session

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=> NMR and Bcl-2
           1   FILE ADISINSIGHT
           2   FILE AGRICOLA
           1   FILE BIOENG
          39   FILE BIOSIS
           4   FILE BIOTECHABS
           4   FILE BIOTECHDS
          10   FILE BIOTECHNO
          17   FILE CANCERLIT
          49   FILE CAPLUS
           1   FILE CEABA-VTB
           2   FILE CIN
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           3   FILE DDFU
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           5   FILE DRUGU
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          22   FILE ESBIOBASE
           3   FILE FEDRIP
  36 FILES SEARCHED...
           1   FILE FSTA
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           8   FILE LIFESCI
          37   FILE MEDLINE
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           1   FILE PROMT
          55   FILE SCISEARCH
          16   FILE TOXCENTER
         546   FILE USPATFULL
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           3   FILE WPIDS
  73 FILES SEARCHED...
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  31 FILES HAVE ONE OR MORE ANSWERS,   75 FILES SEARCHED IN STNINDEX

L1    QUE NMR AND BCL-2

=> NMR p Bcl-2
  32 FILES SEARCHED...
  68 FILES SEARCHED...

   0 FILES HAVE ONE OR MORE ANSWERS,   75 FILES SEARCHED IN STNINDEX

L2    QUE NMR P BCL-2

=> NMR and Bcl-2 and TR3
           1   FILE BIOTECHABS
           1   FILE BIOTECHDS
           1   FILE CAPLUS
  27 FILES SEARCHED...
           1   FILE IFIPAT
  48 FILES SEARCHED...
           4   FILE USPATFULL
  69 FILES SEARCHED...
           1   FILE WPIDS
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1 FILE WPINDEX

7 FILES HAVE ONE OR MORE ANSWERS, 75 FILES SEARCHED IN STNINDEX

L3 QUE NMR AND BCL-2 AND TR3

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	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	6.27	6.48

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=> NMR and Bcl-2 and TR3
L4 5 NMR AND BCL-2 AND TR3

=> dup remove
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PROCESSING COMPLETED FOR L4
L5 5 DUP REMOVE L4 (0 DUPLICATES REMOVED)

=> d ti 1-5

L5 ANSWER 1 OF 5 USPATFULL on STN
TI Conversion of apoptotic proteins

L5 ANSWER 2 OF 5 USPATFULL on STN
TI Therapeutic treatment methods

L5 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN
TI Conversion of apoptotic proteins

L5 ANSWER 4 OF 5 USPATFULL on STN
TI Blood cell deficiency treatment method

L5 ANSWER 5 OF 5 USPATFULL on STN
TI Isolated nucleic acid encoding a ubiquitous nuclear receptor

=> d ab bib 2, 4, 5

L5 ANSWER 2 OF 5 USPATFULL on STN
AB The invention relates to the use of compounds to ameliorate or treat an condition such as a cystic fibrosis, neutropenia or other exemplified conditions. Exemplary compounds that can be used include 3β-hydroxy-17β-aminoandrost-5-ene, 3β-hydroxy-16α-fluoro-17β-aminoandrost-5-ene, 3α-hydroxy-16α-fluoro-17β-aminoandrost-5-ene, 3β-hydroxy-16β-fluoro-17β-aminoandrost-5-ene, 1α,3β-dihydroxy-4α-fluoroandrost-5-ene-17-one, 1α,3β,17β-trihydroxy-4α-fluoroandrost-5-ene, 1β,3β-dihydroxy-6α-bromoandrost-5-ene,

1α-fluoro-3β,12α-dihydroxyandrost-5-ene-17-one,
1α-fluoro-3β,4α-dihydroxyandrost-5-ene and
4α-fluoro-3β,6α,17β-trihydroxyandrostane.
AN 2004:179017 USPATFULL
TI Therapeutic treatment methods
IN Reading, Christopher L., San Diego, CA, UNITED STATES
Ahlem, Clarence N., San Diego, CA, UNITED STATES
Auci, Dominick L., San Diego, CA, UNITED STATES
Dowding, Charles, San Diego, CA, UNITED STATES
Frincke, James M., San Diego, CA, UNITED STATES
Li, Mei, San Diego, CA, UNITED STATES
Page, Theodore M., Carlsbad, CA, UNITED STATES
Stickney, Dwight R., Granite Bay, CA, UNITED STATES
Trauger, Richard J., Leucadia, CA, UNITED STATES
White, Steven K., San Diego, CA, UNITED STATES
PI US 2004138187 A1 20040715
AI US 2003-651515 A1 20030828 (10)
PRAI US 2002-407146P 20020828 (60)
US 2002-408332P 20020904 (60)
US 2003-479257P 20030617 (60)
DT Utility
FS APPLICATION
LREP HOLLIS-EDEN PHARMACEUTICALS, INC., 4435 EASTGATE MALL, SUITE 400, SAN DIEGO, CA, 92121
CLMN Number of Claims: 37
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 16128
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 4 OF 5 USPATFULL on STN
AB The invention relates to the use of compounds to treat a number of conditions, such as thrombocytopenia, neutropenia or the delayed effects of radiation therapy. Compounds that can be used in the invention include methyl-2,3,4-trihydroxy-1-O-(7,17-dioxoandrost-5-ene-3β-yl)-β-D-glucopyranosiduronate, 16α,3α-dihydroxy-5α-androstan-17-one or 3,7,16,17-tetrahydroxyandrost-5-ene, 3,7,16,17-tetrahydroxyandrost-4-ene,3,7,16,17-tetrahydroxyandrost-1-ene or 3,7,16,17-tetrahydroxyandrostane that can be used in the treatment method.
AN 2003:120747 USPATFULL
TI Blood cell deficiency treatment method
IN Ahlem, Clarence N., San Diego, CA, UNITED STATES
Reading, Christopher, San Diego, CA, UNITED STATES
Frincke, James, San Diego, CA, UNITED STATES
Stickney, Dwight, Granite Bay, CA, UNITED STATES
Lardy, Henry A., Madison, WI, UNITED STATES
Marwah, Padma, Middleton, WI, UNITED STATES
Marwah, Ashok, Middleton, WI, UNITED STATES
Prendergast, Patrick T., Straffan, IRELAND
PI US 2003083231 A1 20030501
AI US 2002-87929 A1 20020301 (10)
RLI Continuation-in-part of Ser. No. US 2000-675470, filed on 28 Sep 2000, PENDING Continuation-in-part of Ser. No. US 2001-820483, filed on 29 Mar 2001, PENDING Continuation-in-part of Ser. No. US 2000-535675, filed on 23 Mar 2000, PENDING Continuation-in-part of Ser. No. US 1999-449004, filed on 24 Nov 1999, ABANDONED Continuation-in-part of Ser. No. US 1999-449184, filed on 24 Nov 1999, ABANDONED Continuation-in-part of Ser. No. US 1999-449042, filed on 24 Nov 1999, ABANDONED

Continuation-in-part of Ser. No. US 1999-461026, filed on 15 Dec 1999, ABANDONED Continuation-in-part of Ser. No. US 2000-586673, filed on 1 Jun 2000, ABANDONED Continuation-in-part of Ser. No. US 2000-586672, filed on 1 Jun 2000, ABANDONED Continuation-in-part of Ser. No. US 1999-414905, filed on 8 Oct 1999, ABANDONED

PRAI US 1999-161453P 19991025 (60)
US 2001-272624P 20010301 (60)
US 2001-323016P 20010911 (60)
US 2001-340045P 20011130 (60)
US 2001-328738P 20011011 (60)
US 2001-338015P 20011108 (60)
US 2001-343523P 20011220 (60)
US 1999-126056P 19991019 (60)
US 1999-124087P 19990311 (60)
US 1998-109923P 19981124 (60)
US 1998-109924P 19981124 (60)
US 1998-110127P 19981127 (60)
US 1998-112206P 19981215 (60)
US 1999-145823P 19990727 (60)
US 1999-137745P 19990603 (60)
US 1999-140028P 19990616 (60)

DT Utility
FS APPLICATION
LREP HOLLIS-EDEN PHARMACEUTICALS, INC., 4435 EASTGATE MALL, SUITE 400, SAN DIEGO, CA, 92121
CLMN Number of Claims: 45
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 19428
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 5 OF 5 USPATFULL on STN

AB The invention relates generally to compositions of and methods for obtaining ubiquitous, nuclear receptor (UR) polypeptides. The invention also relates to polynucleotides encoding UR polypeptides, recombinant host cells and vectors containing UR-encoding polynucleotide sequences, and recombinant UR polypeptides. By way of example, the invention discloses the cloning and functional expression of at least two different UR polypeptides. The invention also includes methods for using the isolated, recombinant receptor polypeptides in assays designed to select substances which interact with UR polypeptides for use in diagnostic, drug design and therapeutic applications.

AN 97:51869 USPATFULL
TI Isolated nucleic acid encoding a ubiquitous nuclear receptor
IN Liao, Shutsung, Chicago, IL, United States
Song, Ching, Durham, NC, United States
PA Arch Development Corporation, Chicago, IL, United States (U.S. corporation)
PI US 5639616 19970617
AI US 1994-342411 19941118 (8)
RLI Continuation-in-part of Ser. No. US 1993-152003, filed on 10 Nov 1993, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Walsh, Stephen G.; Assistant Examiner: Ulm, John D.
LREP Arnold White & Durkee
CLMN Number of Claims: 17
ECL Exemplary Claim: 1
DRWN 21 Drawing Figure(s); 18 Drawing Page(s)

08/11/200414:05Print selected from Online session

LN.CNT 4472
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> index bioscience
FILE 'DRUGMONOG' ACCESS NOT AUTHORIZED
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	16.25	22.73

INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, ANTE, AQUALINE, AQUASCI, BIOBUSINESS, BIOCOMMERCE, BIOENG, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE, DISSABS, ...' ENTERED AT 13:33:39 ON 08 NOV 2004

75 FILES IN THE FILE LIST IN STNINDEX

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=> Bcl-2 and NMR and apoptosis
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          1   FILE ADISINSIGHT
          2   FILE AGRICOLA
          1   FILE BIOENG
         22   FILE BIOSIS
          0*  FILE BIOTECHABS
  13 FILES SEARCHED...
          2   FILE BIOTECHDS
          8   FILE BIOTECHNO
         10   FILE CANCERLIT
         29   FILE CAPLUS
          1   FILE CEABA-VTB
          1   FILE CIN
          3   FILE DDFU
          3   FILE DISSABS
          5   FILE DRUGU
         21   FILE EMBASE
  33 FILES SEARCHED...
         15   FILE ESBIOBASE
          3   FILE FEDRIP
          1   FILE FSTA
          6   FILE IFIPAT
          4   FILE JICST-EPLUS
          6   FILE LIFESCI
         25   FILE MEDLINE
          3   FILE NTIS
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          8   FILE TOXCENTER
        466   FILE USPATFULL
         44   FILE USPAT2
          2   FILE WPIDS
  73 FILES SEARCHED...
          2   FILE WPINDEX

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L6 QUE BCL-2 AND NMR AND APOPTOSIS

=>

=>

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=> d rank

F1	466	USPATFULL
F2	44	SCISEARCH
F3	44	USPAT2
F4	29	CAPLUS
F5	25	MEDLINE
F6	22	BIOSIS
F7	21	EMBASE
F8	15	ESBIOBASE
F9	10	CANCERLIT
F10	8	BIOTECHNO
F11	8	TOXCENTER
F12	7	PASCAL
F13	6	IFIPAT
F14	6	LIFESCI
F15	5	DRUGU
F16	4	JICST-EPLUS
F17	3	DDFU
F18	3	DISSABS
F19	3	FEDRIP
F20	3	NTIS
F21	2	AGRICOLA
F22	2	BIOTECHDS
F23	2	WPIDS
F24	2	WPINDEX
F25	1	ADISINSIGHT
F26	1	BIOENG
F27	1	CEABA-VTB
F28	1	CIN
F29	1	FSTA
F30	1	PROMT

=> file biosis medline caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	10.83	33.56

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=> Bcl-2 and NMR and apoptosis
L7 76 BCL-2 AND NMR AND APOPTOSIS

=> dup remove
ENTER L# LIST OR (END):l7
PROCESSING COMPLETED FOR L7
L8 43 DUP REMOVE L7 (33 DUPLICATES REMOVED)

=> d ti 1-23

L8 ANSWER 1 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
TI Conversion of apoptotic proteins

L8 ANSWER 2 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
TI Methods of identifying agents that alter association of Bit1 and AES, alter **Bcl-2** transcription, and/or modulate cell death, and therapeutic uses

L8 ANSWER 3 OF 43 MEDLINE on STN
TI Conformation of membrane-associated proapoptotic tBid.

L8 ANSWER 4 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
TI Changes in phosphate metabolism in thymoma cells suggest mechanisms for resistance to dexamethasone-induced **apoptosis**. A 31P **NMR** spectroscopic study of cell extracts. [Erratum to document cited in CA138:036909]

L8 ANSWER 5 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
TI Solution Conformations of Wild-Type and Mutated Bak BH3 Peptides via Dynamical Conformational Sampling and Implication to Their Binding to Antiapoptotic **Bcl-2** Proteins

L8 ANSWER 6 OF 43 MEDLINE on STN DUPLICATE 1
TI Targeting **apoptosis** via chemical design: inhibition of bid-induced cell death by small organic molecules.

L8 ANSWER 7 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 2
TI Divergence of Genbank and human tumor **Bcl-2** sequences and implications for binding affinity to key apoptotic proteins.

L8 ANSWER 8 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 3
TI Localization of dynein light chains 1 and 2 and their pro-apoptotic ligands.

L8 ANSWER 9 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 4
TI Rational design and real time, in-cell detection of the proapoptotic activity of a novel compound targeting Bcl-XL.

L8 ANSWER 10 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 5
TI Small-molecule inhibitors of **Bcl-2** protein.

L8 ANSWER 11 OF 43 MEDLINE on STN DUPLICATE 6
TI Structural studies of **apoptosis** and ion transport regulatory proteins in membranes.

L8 ANSWER 12 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 7
TI Defining the p53 DNA-binding domain/Bcl-xL-binding interface using **NMR**.

L8 ANSWER 13 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 8
TI Overexpression of catalase or **Bcl-2** alters glucose and energy metabolism concomitant with dexamethasone resistance.

L8 ANSWER 14 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
TI Humanin protein interactions with Bax and Bid and their use for identifying modulators of **apoptosis**

L8 ANSWER 15 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
TI Solution Structure of Human BCL-w: Modulation of Ligand Binding by the C-Terminal Helix

L8 ANSWER 16 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
TI Discovery, Characterization, and Structure-Activity Relationships Studies of Proapoptotic Polyphenols Targeting B-Cell Lymphocyte/Leukemia-2 Proteins

L8 ANSWER 17 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
TI Cyclic AMP reverses radiocontrast media-induced **apoptosis** in LLC-PK1 cells by activating A kinase/PI3 kinase

L8 ANSWER 18 OF 43 MEDLINE on STN
TI Unique structural features of a **BCL-2** family protein CED-9 and biophysical characterization of CED-9/EGL-1 interactions.

L8 ANSWER 19 OF 43 MEDLINE on STN
TI Solution structure of the BHRF1 protein from Epstein-Barr virus, a homolog of human **Bcl-2**.

L8 ANSWER 20 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI Interaction of BID, a pro-apoptotic **BCL-2** family member, with lipid membranes: A site-directed spin labeling Study.

L8 ANSWER 21 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 9
TI Overexpression of catalase or **Bcl-2** delays or prevents alterations in phospholipid metabolism during glucocorticoid-induced **apoptosis** in WEHI7.2 cells.

L8 ANSWER 22 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 10
TI Structure determination, **apoptosis** induction, and telomerase inhibition of CFP-2, a novel lichenin from Cladonia furcata.

L8 ANSWER 23 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI Novel chemically-stabilized helices of the **BCL-2** family induce **apoptosis** of leukemia cells.

=> d ab bib 23

L8 ANSWER 23 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

AB Faulty regulation of apoptotic pathways is a seminal event in the pathogenesis of a wide variety of hematologic, oncologic, and other diseases. **Apoptosis** is governed by the **BCL-2** family of pro- and anti-apoptotic proteins, which form a complex network of checks and balances that dictate cell fate. **BCL-2**, for example, is a survival protein whose overproduction can facilitate pathologic cell survival. Anti-apoptotic proteins, such as **BCL-2** and BCL-XL, and pro-apoptotic proteins, such as BAK and BAX, share sequence conservation in multiple "**BCL-2** homology" (BH) domains. These "multidomain" apoptotics exert their roles as guardian or executioner at mitochondrial and endoplasmic reticulum membranes, receiving regulatory signals from another class of pro-apoptotic proteins, characterized by homology in the BH3-domain only. Deletion and mutagenesis studies determined that the amphipathic alpha-helical BH3 segment of pro-apoptotic family members functions as a critical death domain. Whereas peptides modeled after BH3 domains retain select in vitro biochemical activities, their in vivo utility is compromised by loss of helical secondary structure, susceptibility to proteolytic degradation, and inability to penetrate intact cells. We developed and applied a chemical strategy for generating highly specific and stable peptidic compounds that preserve both the primary and secondary structure of biologically active apoptotic peptides, in order to maximize their potential as therapeutic reagents and as in vivo biological tools to elucidate apoptotic pathways. We employed a synthetic crosslinking strategy to generate a panel of "Stabilized Alpha-Helices of BH3-domains" or SAHBs modeled after the BH3 domain of BID, a pro-apoptotic family member capable of activating mitochondrial cell death through interactions with both pro- and anti-apoptotic multidomain proteins. Circular dichroism studies revealed dramatic enhancement of SAHB secondary structure in solution, with several compounds displaying a more than 5-fold increase in percent helicity compared to the unmodified BID BH3 peptide. SAHBs are likewise more resistant to proteolytic degradation as determined by trypsin digestion kinetic analyses. In in vitro binding assays, SAHBs display increased **BCL-2** binding affinity. Two-dimensional 1H-15N Heteronuclear Single Quantum Correlation Nuclear Magnetic Resonance (HSQC **NMR**) spectra confirmed that SAHBs specifically engage the physiologic BH3-binding site of multidomain anti-apoptotic proteins. SAHBs induce rapid release of cytochrome c from purified mouse liver mitochondria, but have no effect on mitochondria lacking BAK/BAX, confirming the specificity of SAHB activity in triggering mitochondrial **apoptosis**. The cell permeability of SAHBs was demonstrated by tracking fluorescein-labeled SAHBs in cultured cells by FACS analysis and confocal microscopy. Furthermore, SAHBs activate **apoptosis** in cultured B-, T-, and mixed-lineage leukemia cells. The specificity of SAHB activity in inducing leukemia cell **apoptosis** was confirmed by the inability of mutant SAHBs, incorporating a single point mutation known to abolish BH3-domain activity, to have any effect on the cultured cells. These data indicate that SAHBs have the potential to serve as biological tools to dissect and manipulate apoptotic pathways in vivo in normal and malignant cells.

AN 2004:180831 BIOSIS

DN PREV200400180880

TI Novel chemically-stabilized helices of the **BCL-2** family induce **apoptosis** of leukemia cells.

AU Walensky, Loren D. [Reprint Author]; Escher, Iris; Malia, Thomas J.; Wagner, Gerhard; Verdine, Gregory L.; Korsmeyer, Stanley J.

CS Department of Pediatric Hematology/Oncology, Dana Farber Cancer Institute/Children's Hospital Boston, Harvard Medical School, Boston, MA, USA
SO Blood, (November 16 2003) Vol. 102, No. 11, pp. 5a. print.
Meeting Info.: 45th Annual Meeting of the American Society of Hematology. San Diego, CA, USA. December 06-09, 2003. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 7 Apr 2004
Last Updated on STN: 7 Apr 2004

=> d ti 43-23
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=> d ti 23-43

L8 ANSWER 23 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI Novel chemically-stabilized helices of the **BCL-2** family induce **apoptosis** of leukemia cells.

L8 ANSWER 24 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
TI Phospholipid scramblase transport system-based method for targeting chemical compounds to cells, pharmaceutical compositions, and therapeutic and diagnostic use

L8 ANSWER 25 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of amino acid derivatives used as perturbed membrane-binding compounds for diagnostic and therapeutic applications

L8 ANSWER 26 OF 43 MEDLINE on STN
TI The apoptotic protein tBid promotes leakage by altering membrane curvature.

L8 ANSWER 27 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 11
TI Novel polyphenol molecule isolated from licorice root (Glycrrhiza glabra) induces **apoptosis**, G2/M cell cycle arrest, and **Bcl-**

2 phosphorylation in tumor cell lines.

L8 ANSWER 28 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI A view to a kill: Ligands for **Bcl-2** family proteins.

L8 ANSWER 29 OF 43 MEDLINE on STN DUPLICATE 12
TI Changes in phosphate metabolism in thymoma cells suggest mechanisms for resistance to dexamethasone-induced **apoptosis**. A 31P **NMR** spectroscopic study of cell extracts.

L8 ANSWER 30 OF 43 MEDLINE on STN
TI Backbone dynamics of the 8 kDa dynein light chain dimer reveals molecular basis of the protein's functional diversity.

L8 ANSWER 31 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 13
TI Novel substituted methylenedioxy lignan suppresses proliferation of cancer cells by inhibiting telomerase and activation of c-myc and caspases leading to **apoptosis**.

L8 ANSWER 32 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 14
TI What's in the 'BAG'?: A functional domain analysis of the BAG-family proteins.

L8 ANSWER 33 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 15
TI Discovery of small-molecule inhibitors of **Bcl-2** through structure-based computer screening.

L8 ANSWER 34 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI Bax and other pro-apoptotic **Bcl-2** family "killer-proteins" and their victim, the mitochondrion.

L8 ANSWER 35 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 16
TI Identification of small-molecule inhibitors of interaction between the BH3 domain and Bcl-xL.

L8 ANSWER 36 OF 43 MEDLINE on STN
TI **NMR** studies of the anti-apoptotic protein Bcl-xL in micelles.

L8 ANSWER 37 OF 43 MEDLINE on STN
TI Rationale for Bcl-xL/Bad peptide complex formation from structure, mutagenesis, and biophysical studies.

L8 ANSWER 38 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI Targeting the mitochondrial redox state of leukemia and lymphoma cells with PK11195 for effective therapy.

L8 ANSWER 39 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI Assessing pore formation by **BCL-2** during **apoptosis** in cell lines and human leukemic cells: Cysteine 158 in the alpha 5 helical loop is in an aqueous environment.

L8 ANSWER 40 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 17
TI Refolding, purification, and characterization of a loop deletion mutant of human **Bcl-2** from bacterial inclusion bodies.

L8 ANSWER 41 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 18
TI Recombinant mouse **Bcl-2**-(1-203): Two domains connected by a long protease-sensitive linker.

L8 ANSWER 42 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 19
TI Detection of apoptotic cell death by proton nuclear magnetic resonance spectroscopy.

L8 ANSWER 43 OF 43 MEDLINE on STN
TI X-ray and **NMR** structure of human Bcl-xL, an inhibitor of programmed cell death.

=> d ti 29, 34, 37, 42, 43

L8 ANSWER 29 OF 43 MEDLINE on STN DUPLICATE 12
TI Changes in phosphate metabolism in thymoma cells suggest mechanisms for resistance to dexamethasone-induced **apoptosis**. A 31P **NMR** spectroscopic study of cell extracts.

L8 ANSWER 34 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI Bax and other pro-apoptotic **Bcl-2** family "killer-proteins" and their victim, the mitochondrion.

L8 ANSWER 37 OF 43 MEDLINE on STN
TI Rationale for Bcl-xL/Bad peptide complex formation from structure, mutagenesis, and biophysical studies.

L8 ANSWER 42 OF 43 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 19
TI Detection of apoptotic cell death by proton nuclear magnetic resonance spectroscopy.

L8 ANSWER 43 OF 43 MEDLINE on STN
TI X-ray and **NMR** structure of human Bcl-xL, an inhibitor of programmed cell death.

=> d ab bib 29, 34, 37, 42, 43

L8 ANSWER 29 OF 43 MEDLINE on STN DUPLICATE 12
AB Treatment of the mouse thymoma-derived WEHI7.2 cell line with dexamethasone, a synthetic glucocorticoid, causes the cells to undergo **apoptosis**. Previous studies have shown that WEHI7.2 cell variants with an increased antioxidant defense exhibit increased resistance to dexamethasone-induced **apoptosis**, suggesting that oxidative stress may play a role in glucocorticoid-induced **apoptosis**. In this work we compared metabolic profiles of WEHI7.2 parental cells with those of WEHI7.2 variants with an increased antioxidant defense or overexpressing **bcl-2**, to determine whether bolstering the antioxidant defense results in altered metabolic parameters that could

translate into increased resistance to dexamethasone-induced **apoptosis**. WEHI7.2 parental cells and cells overexpressing catalase, thioredoxin or **bcl-2**, or selected for resistance to 200 micro M H(2)O(2) were cultured in low-glucose DMEM medium supplemented with 10% calf serum, and extracted using chloroform-methanol-water (1:1:1). Metabolites contained in the aqueous and organic phases of the extracts were processed separately and subjected to high-resolution (31)P **NMR** spectroscopy. In most of the steroid-resistant variants, ATP levels and energetic status were decreased compared with the steroid-sensitive parental cell line, while the concentrations of hexose and triose phosphates were increased. Furthermore, the ratio of choline-containing phospholipids to ethanolamine-containing phospholipids was generally reduced in steroid-resistant cells. Phosphatidylethanolamine and its derivatives contain a higher amount of polyunsaturated fatty acids (PUFA) than the choline-containing analogs, and PUFA are readily oxidized by reactive oxygen species. Therefore, an increased initial amount of phosphatidylethanolamine may increase the 'buffering capacity' of this antioxidant and may thus contribute to the steroid resistance of WEHI7.2 variants.

AN 2002444772 MEDLINE

DN PubMed ID: 12203227

TI Changes in phosphate metabolism in thymoma cells suggest mechanisms for resistance to dexamethasone-induced **apoptosis**. A 31P **NMR** spectroscopic study of cell extracts.

AU Lutz N W; Tome M E; Aiken N R; Briehl M M

CS Arizona Cancer Center, PO Box 245024, University of Arizona, Tucson, AZ 85724, USA.

NC CA 09213 (NCI)
CA 71768 (NCI)
CA 80130 (NCI)

SO NMR in biomedicine, (2002 Aug) 15 (5) 356-66.
Journal code: 8915233. ISSN: 0952-3480.

CY England: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 200303

ED Entered STN: 20020831
Last Updated on STN: 20030321
Entered Medline: 20030320

L8 ANSWER 34 OF 43 BIOSIS on STN

AB Two major intracellular **apoptosis** signaling cascades have been characterized, the mitochondrial pathway and the death receptor pathway. The mitochondrial pathway is regulated by members of the **Bcl-2** protein family. The members of this family can be subdivided into anti- and pro-apoptotic proteins. The pro-apoptotic members are further divided into two groups, the multidomain and the 'BH3 domain only' proteins. When cells are exposed to apoptotic stimulation, pro-apoptotic proteins are activated through post-translational modifications or changes in their conformation. The main site of action of the multidomain proteins are the mitochondria, where these proteins induce permeabilization of the outer membrane resulting in the release of proteins, including cytochrome c, from the intermembrane space. In the cytosol cytochrome c activates caspase cascades ultimately leading to cell death. Mounting evidence indicates that **apoptosis** is involved

in a wide range of pathological conditions. Recent studies suggest that the mitochondrial signaling pathway is involved in several diseases. Although, so far, with the exception of C. elegans, most studies on **apoptosis** have been performed in mammalian systems, recently homologues to the **Bcl-2** family members, including pro-apoptotic members, have been identified in Drosophila and zebrafish. Here the structure and function of the various pro-apoptotic **Bcl -2** family members, their effects on mitochondria, and their involvement in diseases are discussed.

AN 2002:270954 BIOSIS
DN PREV200200270954
TI Bax and other pro-apoptotic **Bcl-2** family "killer-proteins" and their victim, the mitochondrion.
AU Antonsson, Bruno [Reprint author]
CS Serono Pharmaceutical Research Institute, 14, chemin des Aulx, 1228 Plan-les-Ouates, Geneva, Switzerland
bruno.antonsson@serono.com
SO Cell and Tissue Research, (December, 2001) Vol. 306, No. 3, pp. 347-361. print.
CODEN: CTSRCS. ISSN: 0302-766X.
DT Article
General Review; (Literature Review)
LA English
ED Entered STN: 1 May 2002
Last Updated on STN: 1 May 2002

L8 ANSWER 37 OF 43 MEDLINE on STN
AB The three-dimensional structure of the anti-apoptotic protein Bcl-xL complexed to a 25-residue peptide from the death promoting region of Bad was determined using **NMR** spectroscopy. Although the overall structure is similar to Bcl-xL bound to a 16-residue peptide from the Bak protein (Sattler et al., 1997), the Bad peptide forms additional interactions with Bcl-xL. However, based upon site-directed mutagenesis experiments, these additional contacts do not account for the increased affinity of the Bad 25-mer for Bcl-xL compared to the Bad 16-mer. Rather, the increased helix propensity of the Bad 25-mer is primarily responsible for its greater affinity for Bcl-xL. Based on this observation, a pair of 16-residue peptides were designed and synthesized that were predicted to have a high helix propensity while maintaining the interactions important for complexation with Bcl-xL. Both peptides showed an increase in helix propensity compared to the wild-type and exhibited an enhanced affinity for Bcl-xL.

AN 2001300585 MEDLINE
DN PubMed ID: 11206074
TI Rationale for Bcl-xL/Bad peptide complex formation from structure, mutagenesis, and biophysical studies.
AU Petros A M; Nettesheim D G; Wang Y; Olejniczak E T; Meadows R P; Mack J; Swift K; Matayoshi E D; Zhang H; Thompson C B; Fesik S W
CS Pharmaceutical Discovery Division, Abbott Laboratories, Abbott Park, Illinois 60064-6098, USA.
SO Protein science : a publication of the Protein Society, (2000 Dec) 9 (12) 2528-34.
Journal code: 9211750. ISSN: 0961-8368.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200105
ED Entered STN: 20010604

Last Updated on STN: 20010604
Entered Medline: 20010531

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AB Cells undergoing **apoptosis** (programmed cell death) display profound morphologic and biochemical changes in the nucleus, cytoplasm, and plasma membrane. We have shown a direct temporal relationship between the onset of **apoptosis** in Jurkat T-cell lymphoblast cultures and a greater than twofold increase in the signal intensity of the methylene resonance (at 1.3 ppm) as observed by proton nuclear magnetic resonance spectroscopy (1H **NMR**). The increase in the methylene resonance intensity was seen when **apoptosis** was induced by serum deprivation, glucocorticoid, and doxorubicin treatment but not in necrotic (nonapoptotic) cell death. We have found similar changes in a variety of other cell lines undergoing **apoptosis** including the Hut 78 T-cell leukemia, JY natural killer T-cell leukemia, Daudi B-cell lymphoma, HeLa, and 3T3 fibroblast cell lines. Furthermore, this spectral change was diminished in **Bcl-2** overexpressing HL-60 cell cultures treated with doxorubicin, which were relatively resistant to **apoptosis**, as compared to apoptotic HL-60 cultures. 1H **NMR** spectroscopy therefore may be useful in detecting apoptotic cell death in vivo.

AN 1996:125822 BIOSIS

DN PREV199698697957

TI Detection of apoptotic cell death by proton nuclear magnetic resonance spectroscopy.

AU Blankenberg, Francis G. [Reprint author]; Storrs, Richard W.; Naumovski, Louie; Goralski, Thomas; Spielman, Daniel

CS Lucile Salter Packard Child. Hosp., Dep. Radiol., 725 Welch Rd., Palo Alto, CA 94304, USA

SO Blood, (1996) Vol. 87, No. 5, pp. 1951-1956.
CODEN: BLOOAW. ISSN: 0006-4971.

DT Article

LA English

ED Entered STN: 27 Mar 1996
Last Updated on STN: 27 Mar 1996

L8 ANSWER 43 OF 43 MEDLINE on STN

AB THE **Bcl-2** family of proteins regulate programmed cell death by an unknown mechanism. Here we describe the crystal and solution structures of a **Bcl-2** family member, Bcl-xL (reference 2). The structures consist of two central, primarily hydrophobic alpha-helices, which are surrounded by amphipathic helices. A 60-residue loop connecting helices alpha1 and alpha2 was found to be flexible and non-essential for anti-apoptotic activity. The three functionally important **Bcl-2** homology regions (BH1, BH2 and BH3) are in close spatial proximity and form an elongated hydrophobic cleft that may represent the binding site for other **Bcl-2** family members. The arrangement of the alpha-helices in Bcl-xL is reminiscent of the membrane translocation domain of bacterial toxins, in particular diphtheria toxin and the colicins. The structural similarity may provide a clue to the mechanism of action of the **Bcl-2** family of proteins.

AN 96256675 MEDLINE

DN PubMed ID: 8692274

TI X-ray and **NMR** structure of human Bcl-xL, an inhibitor of programmed cell death.

AU Muchmore S W; Sattler M; Liang H; Meadows R P; Harlan J E; Yoon H S;

Nettesheim D; Chang B S; Thompson C B; Wong S L; Ng S L; Fesik S W
CS Protein Crystallography, Pharmaceutical Discovery Division, Abbott Laboratories, Abbott Park, Illinois 60064, USA.
SO Nature, (1996 May 23) 381 (6580) 335-41.
Journal code: 0410462. ISSN: 0028-0836.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS PDB-1LXL; PDB-1MAZ
EM 199608
ED Entered STN: 19960911
Last Updated on STN: 19960911
Entered Medline: 19960823